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PRICKRIL, B
EXAMINER

18M2/0504

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ART UNIT	PAPER NUMBER
1811	7

DATE MAILED: 05/04/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 9/6/94 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☑ Notice re Patent Drawing, PTO-948.
3. ☑ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-30 are pending in the application.
   Of the above, claims 23-25 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-22 and 26-30 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

Part III DETAILED ACTION

Claims 1-22 and 26-30 are pending in this application. Claims 23-25 are withdrawn from consideration as being drawn to a nonelected invention.

Election/Restriction

15. Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group I. Claims 1-22 and 26-30, drawn to pharmaceutical compositions, classified in Class 514, subclass 2.

Group II. Claims 23-25, drawn to processes for the manufacture of pharmaceutical compositions, classified in Class 530, subclass 300.

The inventions are distinct, each from the other because of the following reasons:

16. Inventions of Group I and Group II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (M.P.E.P. § 806.05(f)). In the instant case the process can be used to make a materially different product such as antibiotic preparations.

17. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

18. During a telephone conversation with Janis Fraser on April 25, 1995 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-22 and 26-30. Affirmation of this election must be made by applicant in responding to this Office action. Claims 23-25 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

Specification

19. The disclosure is objected to because of the following informalities:

The first entries under the column headings of Table I on page 22 are either missing or inconsistent with the information provided for other entries in the table. The column heading on the right of the table is illegible. Appropriate correction is required.

Claim rejections

Claims 2, 4, 12, and 27 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is confusing because no antecedent basis exists for the term "resultant powder", i.e., no process is described from which a powder results. The meaning of "coarse particles" is also unclear as to what particle size range is encompassed by this definition.

Claims 4 and 27 are indefinite as to the abbreviations used for atrial natriuretic peptide (hANP), gonadotropin agonist analogs (GnRHa), and thyroxine releasing hormone (TRHrh). Does "h" in these abbreviations refer to "human"; similarly, if "r" and "a" are intended to connote specific meanings such as "recombinant" or "analogs" the full name should recite this fact. What limitations, if any, are to be placed on "analogs" of gonadotropin agonists or somatostatin.

In claim 12 the meaning of a "bile salt derivative" is unclear. For example, it is unclear just what structural changes in bile salts would produce compounds still acceptable as "derivatives".

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

21. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

22. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 86 S.Ct. 684, 15 L.Ed. 2nd 545 (1966), 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103 are summarized as follows:

1. Determining the scope and contents of the prior art;
2. Ascertaining the differences between the prior art and the claims at issue; and
3. Resolving the level of ordinary skill in the pertinent art.

23. Claims 1-14, 17-22, and 26-29 are rejected under 35 U.S.C. § 102(e) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Platz et al. [U.S. Patent No. 5,284,656].

Platz et al. disclose pharmaceutical compositions containing a pharmaceutically active polypeptide and an absorption enhancer for administration via a dry powder inhaler device which are identical to those disclosed by applicants. Even if the pharmaceutical composition and/or inhaler device were not identical to those described by applicants, one of ordinary skill in the peptide art would be motivated to substitute many other biologically active

polypeptides for those described by Platz et al., including the peptides listed by applicants. All of the peptides listed by applicants for use in their invention are well known in the art, and it would be obvious to the skilled artisan to use any of them in a dry powder inhaler device like that disclosed by Platz or many others in order to obtain the advantages of ease of administration and dosage control inherent in this mode of administration. As to the presence of absorption enhancers, Platz et al. give examples thereof, including the fatty acid oleic acid and the phospholipid lecithin; one of ordinary skill in the peptide art would be motivated to substitute other surfactants such as bile salts and phospholipids which are well known in the art to aid metabolic absorption processes. As to the choice of inhaler devices, Platz et al. are careful to point out that a multitude of devices are commercially available, so that one of ordinary skill in the art would be motivated to choose, for example, single or multiple dose devices dependent on the malady to be treated, subject age and condition, and other features well known in the art. Therefore it would have been obvious to one of ordinary skill in the peptide art to substitute the polypeptides, enhancers, and inhaler devices disclosed by applicants for those of Platz et al. in order to obtain the advantages of ease of administration and improved dosage control described by Platz et al.

24. Claims 1-3, 5-11, 17, 18, 21, 22, 26, and 28 are rejected under 35 U.S.C. § 103 as being unpatentable over Rubsamen [U.S. Patent No. 5,364,838] in view of Platz et al. [U.S. Patent No. 5,284,656].

Rubsamen discloses pharmaceutical compositions containing a pharmaceutically active polypeptide and an absorption enhancer, and methods of introducing biologically active polypeptides into the lower respiratory tract of a subject as a dry powder in the presence or absence of a surfactant absorption enhancer via an inhaler device, but Rubsamen does not disclose particle sizes of less than 10 microns. However, Platz et al. disclose methods for administering a dry powder polypeptide formulation containing particles of less than 10 microns via an inhaler device, Therefore, it would have been obvious to one skilled in the art at the time the invention was made to modify the methods of Rubsamen such that they included particle sizes of less than 10 microns so that the advantages of higher absorption and even dosages would be realized, as per the teachings of Platz et al.

25. Claims 1, 2, 6-18, 21, 22, and 28-30 are rejected under 35 U.S.C. § 103 as being unpatentable over Rubsamen [U.S. Patent No. 5,364,838] in view of Clark et al. [U.S. Patent No. 5,341,800] and further in view of Edman et al. [Advanced Drug Delivery Reviews 8, 165-177 (1992)] and Mishima et al. [J. Pharmacol.-Dyn. 10, 624-631(1987)].

Rubsamen discloses methods of introducing insulin into the lower respiratory tract of a subject as a dry powder in the presence of an absorption enhancer, but Rubsamen does not disclose dry powder formulations containing particles of less than 10 microns with a pharmaceutically acceptable carrier capable of forming an ordered mixture in which 50 % of the particles have a diameter of less than 10 microns, or the use of bile salts, phospholipids,

alkyl glycosides, cyclodextrins, or salts of a fatty acid including capric acid as absorption enhancers. However, Clark et al. disclose methods for administering a dry powder formulation via an inhaler device in which 50 % of the particles are less than 10 microns and the particles are capable of forming an ordered mixture, Edman et al. disclose the use of bile salts, phospholipids, alkyl glycosides, cyclodextrins, or fatty acids as absorption enhancers, and Mishima discloses the use of capric acid or its salt as an absorption enhancer, so that the advantages of enhanced absorption and reproducible dosage resulting from these modifications could be realized. Therefore, it would have been obvious to one skilled in the art at the time the invention was made to modify the methods of Rubsamen such that they included formulations in which 50 % of the particles are less than 10 microns, use bile salts, phospholipids, alkyl glycosides, cyclodextrins, or fatty acids as absorption enhancers, and capric acid or its salt as absorption enhancers so that the advantages of higher absorption and even dosages would be realized, as per the teachings of Clark et al. and Mishima et al.

Double Patenting

Claims 1, 2, and 6-19 are provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 1-38 of copending application Serial No. 08/265372. This is a *provisional* double patenting rejection since the conflicting claims have not in fact been patented.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benet Prickril, who can be reached at (703) 305-5933 or by e-mail at "prickril@uspto.gov". The examiner can normally be reached Monday through Thursday between 7:30 AM and 5:00 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached at (703) 308-4037. The fax phone number for Art Unit 1811 is (703) 305-7362.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Benet Prickril, Ph.D.
April 27, 1995

JILL WARDEN
SUPERVISORY PATENT EXAMINER
GROUP 1800